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EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT PAPER NUMBER

1624

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/825,925

Applicant(s)

RAHBAR, SAMUEL

Examiner

Venkataraman Balasubramanian

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-9 is/are allowed.
- 6) ☒ Claim(s) 10-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### **DETAILED ACTION**

Applicants' response, which included amendment to claims 1, 4, 7 and 10 filed on 6/13/2003, is made of record.

Claims 1-12 are pending.

#### ***Terminal Disclaimer***

The terminal disclaimer filed on 6/13/2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of copending application 09/800,976 has been reviewed and is accepted. The terminal disclaimer has been recorded.

In view of applicants' response, particularly amendment to claims 1, 4, 7 and 10 to limit method of use to compounds LR-102 & LR-99, prior art 103 rejection and the obviousness-type double patenting rejection over US 6,337,350, made in the previous office action have been obviated. In addition, in view of applicants' filing of terminal disclaimer along with the above said amendment, the provisional double patenting rejection over copending application 09/800,976, has been obviated.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the specific diseases and neurotoxicity as due to advanced glycation end products, does not reasonably provide enablement for

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reversing the progression of said diseases or neurotoxicity based on any mode of action. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The following apply:

The instant claims 10-12 are drawn to "reversing disease progression in patient of rheumatoid arthritis, Alzheimer's disease, neurotoxicity or atherosclerosis" for which there is no enabling disclosure. The scope of these claims also includes reversing of any or all neurotoxicity which is not adequately enabled solely based on the advanced glycation end product inhibiting activity of the instant compounds provided in the specification. In addition, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Specification has not provided any evidence or nexus that because of the mode of action of the instant compound, the compound would be useful for reversing disease progression in patient of rheumatoid arthritis, Alzheimer's disease or atherosclerosis" including all or any neurotoxicity.

Further, there is no evidence on record which demonstrates that the in-vitro screening test relied upon is recognized in the art as being reasonably predictive of success in any of the contemplated areas of "reversing disease progression". Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility, and not "warranting further study"). Moreover many if not most of diseases such as Alzheimer's disease,

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arthritis, atherosclerosis etc. are very difficult to treat and at present there is no known drug, which can successfully reverse the course of these diseases, despite the fact that there are many drugs, which can be used for "inflammatory condition". Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288. Also note *Hoffman v. Klaus* 9 USPQ 2d 1657 and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support in vivo uses. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of reversing disease progression solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. References cited in the Information Disclosure Statement do not lend support for reversing disease progression or reversing any or all neurotoxicity.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

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1) The nature of the invention:

The method of use claims 10-12 is drawn to "reversing disease progression in patient of rheumatoid arthritis, Alzheimer's disease, neurotoxicity or atherosclerosis". However, specification provides no support for to method of treating or preventing of any and all complications of diabetes including those yet to be discovered. In fact based on the specification and examples, it appears that the instant compounds are mainly advanced glycation end product inhibitors and may be useful for treating those complication due to diabetes which are positively recited in claims 7-9 wherein advanced glycation end product is implicated.

The evidence presented in this case does not show such utilities related to reversing disease progression, but only warrants further study.

2) The state of the prior art:

There are no known compounds of similar structure, which have been demonstrated shown to be useful reversing progression in patient of rheumatoid arthritis, Alzheimer's disease, neurotoxicity or atherosclerosis". For example, the notion that a compound could be effective reversing disease progression in patient of rheumatoid arthritis, Alzheimer's disease, neurotoxicity or atherosclerosis" because of its in interaction with a single target, in the instant case advanced glycation end product inhibiting activity, in general is absolutely contrary to our current understanding of pharmacological basis of drug design and treatment of diseases. In fact a specific target is often chosen to treat a specific disease or that specific target related diseases. Indeed, applicants'

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instant claims 1-9 rely on this fact for treating specific diabetic complications. Furthermore, the prior art search in the related area does not suggest that because of the mode of action of a compound, as advanced glycation end product inhibiting activity would be useful for reversing progression in patient of rheumatoid arthritis, Alzheimer's disease, neurotoxicity or atherosclerosis".

3) The predictability or lack thereof in the art:

As noted above, although there are several prior art which teach similar compounds as advanced glycation inhibiting activity, they do not teach use of the compound disclosed for reversing progression in patient of rheumatoid arthritis, Alzheimer's disease, neurotoxicity or atherosclerosis" and hence there is no art predictability or assurance that instant compound would do so. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present:

Specification provides no guidance or direction, as to how would one use the instant compound to reversing progression in patient of rheumatoid arthritis, Alzheimer's disease, neurotoxicity or atherosclerosis".

5) The presence or absence of working examples:

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There are no working examples to show that how the instant compound could be used for reversing progression in patient of rheumatoid arthritis, Alzheimer's disease, neurotoxicity or atherosclerosis".

6.The breadth of the claim:

The breadth of the claim is broad enough to include prevention of any or all neurotoxicity including those yet to be discovered for which there is no pharmacological basis or showing in the specification.

7) The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims 10-12.

***Allowable Subject Matter***

Claims 1-9 are allowed. Said claims would be allowed since the method of use based on the mode of action of the species embraced in this claim are not taught or suggested by the art of record or from a search in the relevant art area.

References cited in the Information Disclosure Statement (paper # 9) are made of record.

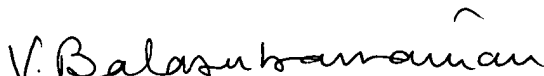
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### Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

  
Venkataraman Balasubramanian

9/6/2003